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REVIEW ARTICLE

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Effectiveness of bed bath methods for skin integrity, skin cleanliness and comfort enhancement in adults: A systematic review

Issei Konya[1] | Kotone Nishiya[1] | Rika Yano[2]

[1]Graduate School of Health Sciences, Hokkaido University, Sapporo, Japan

[2]Faculty of Health Sciences, Hokkaido University, Sapporo, Japan

Correspondence
Rika Yano, Faculty of Health Sciences, Hokkaido University, Kita 12, Nishi 5, Kita-ku, Sapporo, Hokkaido 060-0812, Japan.
Email: r-yano@med.hokudai.ac.jp

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Abstract

Aim: To evaluate the effectiveness of bed bath methods for skin integrity, skin cleanliness and comfort enhancement in adults.

Design: A systematic review based on the PRISMA guidelines.

Methods: We searched for quantitative studies published between 2004–2020, using the PubMed, MEDLINE and CINAHL. The remaining 25 studies were appraised by the JBI tool.

Results: Only four of the included studies were of high quality. Studies of above moderate quality demonstrated that disposable towels were as effective as cotton towels for skin lesions and bacterial removal. Applying a hot towel maintained the skin barrier function and provided warmth; cotton towels were effective for cleaning even with weak pressure, and post-bed bath moisturizer treatment contributed to skin integrity.

Conclusion: Although various methods have been examined, the available evidence is inadequate for establishing best practices. It is necessary to verify empirical research with rigorous methodology involving elderly inpatients and to develop instruments that measure patients' comfort.

KEYWORDS

baths, nurses, nursing care, skin care, systematic review

1 | INTRODUCTION

Bed baths are an integral component of nursing care, frequently performed to maintain the cleanliness of patients who have difficulty taking conventional baths (Perry & Potter, 2017). When correctly performed, this practice supports skin integrity, skin cleanliness and enhanced patient comfort, and the removal of dirt from the skin or mucous membrane (Konya et al., 2020), all of which is done while maintaining skin barrier function (Cowdell et al., 2020). Moreover, bed baths are considered a meaningful hygiene care that strengthens the nurse–patient relationship, and improves the patient's well-being and quality of life (Ahluwalia et al., 2010; Veje et al., 2019).

With the rapid ageing of the global population, the demand for bed baths is expected to increase in hospitals, long-term healthcare facilities and the home care sector. In such circumstances, nurses and caregivers must employ bed bath best practices while drawing on their nursing expertise. Using the larger context of best practices in health care as a reference (Perleth et al., 2001), we have identified best practices as the foremost approach to identifying, collecting, evaluating, disseminating and implementing information about bed

baths for skin integrity, skin cleanliness and comfort enhancement. With this goal in mind, information gleaned from the best available evidence concerning the safety, effectiveness, appropriateness and quality of the bed baths is required.

Previous studies on bed baths have mainly focused on products like towel materials through the lens of skin integrity (Gillis et al., 2016; Groven et al., 2017). Groven et al. (2017) conducted a systematic review that compared traditional bed baths with cotton towels, water and soap to those conducted without water, using disposable towels. Results demonstrated that the latter method is not inferior to the former regarding outcomes for significant skin lesions, patients' resistance to bath and cost.

Still, it is not enough to focus only on towel material. Researchers suggest that skin barrier function can be disrupted by the frictional effects of wiping (Voegeli, 2008). Moreover, excessive wiping friction and force may lead to wounding or tearing of the skin (Bryant & Rolstad, 2001). A systematic review on skin tears and risk factor assessments reported that mechanical factors (i.e. skin care) were significant problems that led to skin tears in clinical settings. It was recommended that nurses and caregivers be trained in employing the correct technique to ensure that they avoid causing skin tears (Serra et al., 2018).

More recently, Cowdell et al. (2020) reported hygiene and emollient-related interventions to maintain the skin integrity in elderly residents within hospital and long-term care settings. It was observed that existing personal hygiene practices for maintaining skin integrity were largely based on tried and tested practice, and the evidence quality was very low. However, the review focused on skin cleansing and emollient products used for bathing, showering and washing—not bed baths, specifically.

Thus, to our knowledge, no comprehensive systematic review of bed bath methods currently exists. Moreover, for accomplishing skin integrity, skin cleanliness and comfort enhancement, bed bath procedural standards have not been determined, specifically in terms of what method, what frequency and for what kind of patient bed baths are most effective. The results of this review are expected to help researchers determine bed bath best practices and contribute to the development of future bed bath research in general. Furthermore, results are expected to contribute to the formulation of suggestions for clinical nursing practice.

2 | AIMS

This systematic review aimed to evaluate and synthesize the effectiveness of evidence-based bed bath methods for skin integrity, skin cleanliness and comfort enhancement in adults.

3 | METHODS

3.1 | Study protocol

A systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Moher et al., 2009) and the Joanna Briggs Institute (JBI) Reviewer's Manual (JBI, 2020). This protocol was not registered in any database in advance. The PRISMA checklist is available in Appendix S1.

3.2 | Inclusion and exclusion criteria

The inclusion and exclusion criteria using the PICOS format (JBI, 2020) are shown in Table 1. This review included all quantitative research papers on bed baths. This wide-ranging approach allows the totality of empirical evidence to be examined and may provide invaluable insight regarding the extent to which results from different study designs complement or contradict each other (JBI, 2020). According to the JBI Reviewer's Manual, qualitative studies cannot employ broad scientific consensus of quantitative systematic reviews; therefore, we did not include these, in order to avoid the heterogeneity and complexity of the integration.

3.3 | Search strategy

Using a three-phase process, we identified relevant articles (JBI, 2020). In the first phase, electronic bibliographic databases (PubMed, MEDLINE and CINAHL) were employed to determine the appropriate keywords among titles and abstracts; thereby, controlled index terms were used to identify relevant articles in these databases. In the second phase, specific searches for each database were performed using these keywords and controlled index terms to identify potentially relevant articles among databases. In the final phase, a full-text screening for grey literature was conducted via a manual search of all the studies' reference lists to identify additional relevant articles. We searched for articles published between January 2004–May 2020 because the most significant achievements in device development emerged from 2004 onwards. A new model of one of the most widely used devices to measure transepidermal water loss (TEWL), which is the gold standard in skin barrier function assessment (Martini et al., 2018), was launched that successfully eliminated some of the limitations of the previous model (Rosado et al. 2005). Thus, the development of skin barrier function measurement tools from 2004 onwards has facilitated improved measurement reliability in bed bath research. The details of the search strategy in the different databases are shown in Appendix S2.

3.4 | Study screening and selection

Using a literature search, 4,161 studies were initially identified. After duplicates were removed, 2,265 studies were screened. Two reviewers (IK and KN) independently screened all the titles and abstracts of the studies identified for review, and 2,235 studies were excluded based on the established exclusion criteria. Of these, 30 underwent full-text review and five studies were excluded; details of

TABLE 1 Inclusion and exclusion criteria using the PICOS format

Criteria	Inclusion	Exclusion
Population	Adults and older people	Non-adults and older people (e.g. newborn baby and infant)
Interventions/ Phenomenon of interest	Bed baths and bed bath methods	Skin care other than bed baths, not focusing bed bath methods, oral cavity care, wipes for environmental equipment, disinfectant wipes (e.g. chlorhexidine gluconate wipes), wound management, neonatal bathing, dry-cleaning care and bed bath educational content
Comparators	Standard practice, alternative intervention and no comparator	No limitations
Outcomes	Outcome for skin integrity, skin cleanliness, comfort enhancement and the others	No limitations
Study design and publication type	Published, peer-reviewed, systematic reviews of quantitative studies, randomized clinical trials, quasi-experimental studies and observational studies	Qualitative studies, case studies and single expert opinion
Publication years	From January 2004–May 2020	Not from January 2004–May 2020
Language	In English	Not in English

Note: PICOS, P = population; I = interventions/phenomenon of interest; C = comparators; O = outcomes; S = study design.

the reasons for exclusion are outlined in Appendix S3. The reviewers discussed the results of the screening and selection process and reached consensus concerning study eligibility. A third researcher (RY) was consulted when the eligibility of the studies was uncertain, resulting in the remaining 25 studies meeting the inclusion criteria. Figure 1 shows the PRISMA flow diagram representing the study search and selection process.

3.5 | Critical appraisal

The critical appraisal for the methodological quality of the studies was performed using the appropriate JBI tool for each study design (JBI, 2017; Table 2). The checklist contained each assessment criterion, according to each study design (Appendix S4). Two reviewers (IK and KN) independently appraised the remaining 25 studies based on the assessment criterion; any disagreements were solved by a third member (RY). Each criterion was given a rating of "yes," "no," "unclear" or "not applicable"; every criterion rated "yes" was given one point. In this manner, the total score was calculated for each study. The inter-rater reliability of the first consensus in the critical appraisal had an intraclass correlation coefficient of 0.848, reflecting "almost perfect reliability."

Papers that met the inclusion criteria were given one of four quality rankings using the JBI appraisal system (JBI, 2014) and the GRADE approach (Schünemann et al., 2013). Systematic reviews and RCTs were ranked as high quality. A quasi-experimental study with a control group was deemed to be of moderate quality. A quasi-experimental study with a single-group pretest–post-test design/cross-sectional study/cohort study was ranked as low quality. Since the JBI does not prescribe an official cut-off point for the assignment of evidence level after critical appraisal, we assumed that some studies would be deemed very low quality from a methodological standpoint. Thus, some papers were downgraded if they scored less than 50%, per the existing research and recommended methods (Porritt et al., 2014). It was determined that decisions about the review's scoring system and its study inclusion cut-off processes should be made in advance. All reviewers came to agreement concerning these issues before critical appraisal commenced.

3.6 | Data extraction and synthesis

Using structured data extraction tables (JBI, 2020), the data consisted of the authors' names, publication year, country, study design, participant characteristics, intervention methods, outcome measures and main findings. The first and second reviewers (IK and KN) independently extracted the required data from included studies; the third reviewer (RY) cross-checked the accuracy of this extracted information.

Due to variations in study design, intervention methods, participants and outcome measures, it was not possible to perform a meta-analysis. Therefore, we performed a systematic search with narrative synthesis. Although there is no prescriptive guidance for presenting narrative synthesis, it is necessary to structuralize the results using data extraction tables (Lockwood & White, 2012). Using this method, we categorized inductively the included studies based on setting of the interventions and outcomes. First, each study was classified into four categories according to the characteristics of the intervention (i.e. bed bath methods). Second, the evidence obtained from these studies was classified by outcome regarding (1) skin integrity, (2) skin cleanliness and (3) comfort enhancement. These classifications correspond to (1) Tissue Integrity: Skin & Mucous Membranes (1101), (2) Self-care: Bathing (0301) or Hygiene (0305) and (3) Comfort Status: Physical (2010) in The Nursing Outcomes Classification (NOC). The NOC is a standardized classification of patient outcomes that evaluate the effects of nursing care for use in practice, education and research (Moorhead et al., 2013). These

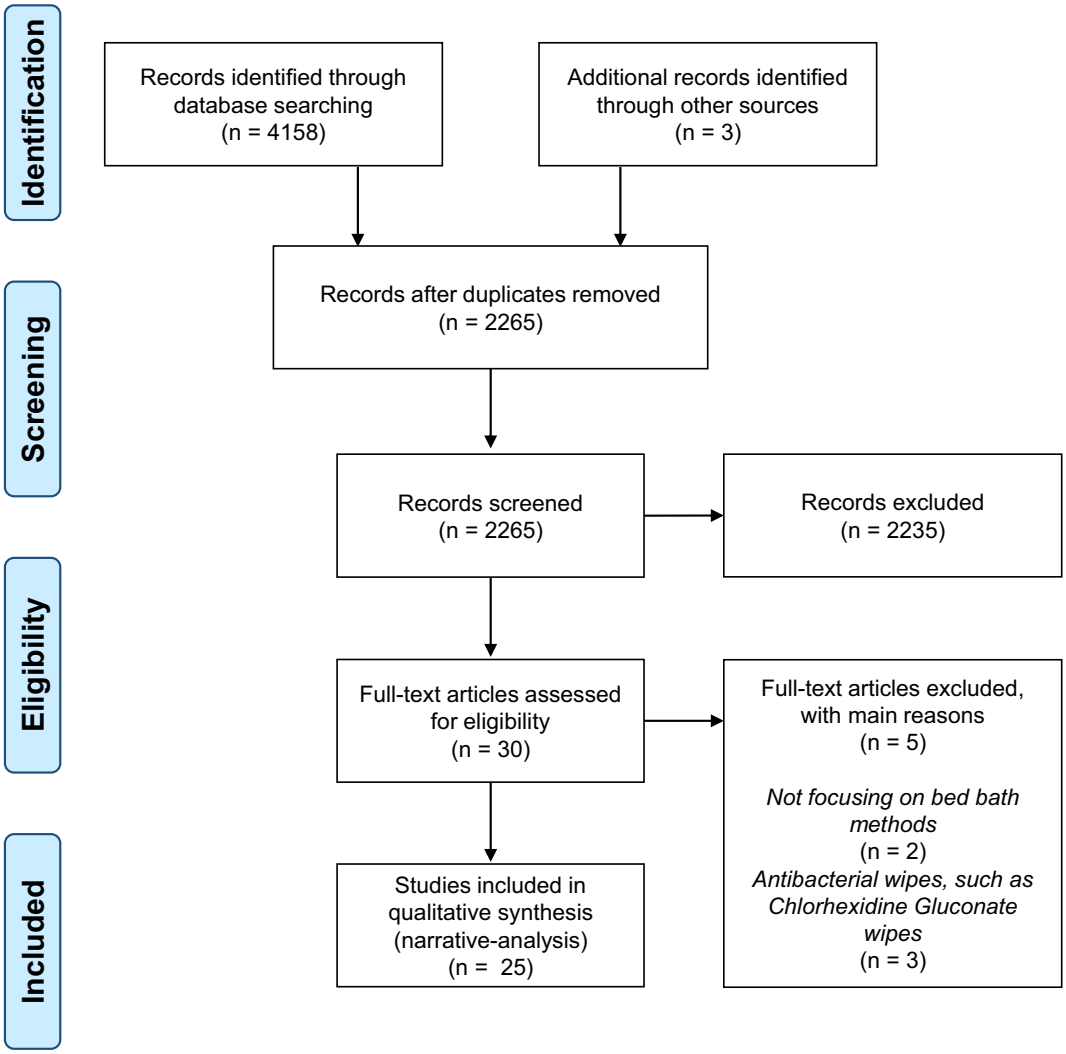

FIGURE 1 PRISMA flow diagram (Moher et al., 2009)

outcome dimensions are also common in skin care research areas (Kottner & Surber, 2016), and the effectiveness of their bed bath methods should be comprehensively evaluated.

4 | RESULTS

4.1 | Outcome measures

Except for two systematic reviews, nine studies measured outcomes for skin integrity. Seven studies measured stratum corneum hydration (SCH, Tables 3-6), and five measured TEWL (Tables 3-6). Two studies measured skin abnormalities (Tables 3 and 7), one measured significant skin lesions (Table 3), and one measured skin pH and skin ceramide (Table 6).

Similarly, 10 studies measured outcomes for skin cleanliness. Seven studies measured microorganisms (Tables 3, 6 and 7). Two studies measured the pseudo-dirt removal rate (Table 5), one measured adenosine triphosphate (Table 5), and one measured the cleaning agent residual index in the lateral surface of the leg (Table 5).

Nine studies measured outcomes for comfort enhancement. Of these, five used a Likert scale for patient satisfaction or subjective evaluation (Tables 3-5). One study used the Profile of Mood States-short form (Table 3), one study used the State-Trait Anxiety Inventory (Table 7) and one study used the Semantic Differential Scale (Table 7).

Eleven studies measured the other outcomes: the time of the bed bath (Tables 3 and 7), costs (Table 3), nurse satisfaction (Table 3), patient resistance (Tables 3 and 7), skin surface temperature (Table 4), axillary temperature (Table 4), the quality of bed bath (Table 3), towel surface temperature (Table 4), vital signs (Tables 4 and 7), Behavioral Pain Scale (Table 7) and bath completeness (Table 7).

4.2 | Characteristics of the included studies

Studies were classified by the intervention characteristics: towel materials ($N = 7$; Table 3), thermal stimulation ($N = 3$; Table 4), wiping ($N = 4$; Table 5), chemical products ($N = 4$; Table 6) and other ($N = 7$;

TABLE 2 Critical appraisal of included studies ($N = 25$)

	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Quality score	Evidence level
Randomized controlled trials															
Gillis et al. (2016)	U	U	○	●	●	●	○	○	●	○	●	●	○	5	M
Schoonhoven et al. (2015)	○	○	○	●	●	●	U	●	○	○	○	○	○	8	H
Sloane et al. (2004)	U	U	○	●	●	○	○	○	●	○	○	●	○	7	H
Systematic reviews and research syntheses															
Cowdell et al. (2020)	○	○	○	○	○	○	○	○	○	○	○			11	H
Groven et al. (2017)	○	○	○	○	○	○	○	○	●	○	○			10	H
Cohort study															
Jury et al. (2011)	●	○	●	○	●	○	●	●	●	●	○			4	VL
Quasi-experimental studies															
Aoki et al. (2019)	○	U	○	○	●	●	○	●	●					4	L
Hayama et al. (2015)	○	○	U	○	○	○	○	●	●					6	M
Jacq et al. (2018)	○	●	●	○	●	○	○	○	●					5	M
Konya et al. (2020)	○	○	○	○	●	○	○	●	○					7	M
Konya, Yamaguchi, et al. (2020)	○	○	○	○	○	○	○	●	○					8	M
Larson et al. (2004)	○	○	U	○	●	●	○	○	●					5	M
Lopes et al. (2010)	○	○	U	○	N/A	○	○	●	●					5	M
Lopes et al. (2013)	○	○	U	○	N/A	○	○	●	○					6	M
Matsumoto et al. (2018)	○	○	○	○	●	U	○	●	●					5	M
Matsumoto et al. (2019)	○	○	○	○	○	●	○	●	●					6	M
Nerandzic et al. (2013)	○	U	U	○	●	U	○	●	●					3	L
Nøddeskou et al. (2015)	○	○	○	○	●	○	○	●	○					7	M
Ogai et al. (2017)	○	○	○	○	○	○	○	○	●					8	M
Shishido et al. (2017)	○	○	○	○	●	○	○	●	○					7	M
Shishido and Yano (2017)	○	○	○	○	○	○	●	●	U					6	M
Silva et al. (2016)	○	U	U	○	●	○	U	○	○					5	M
Veje et al. (2020)	○	○	○	○	●	○	○	○	○					8	M
Analytical cross-sectional studies															
Coyer et al. (2011)	○	○	N/A	○	○	●	○	○						6	L
Matsumura and Fukai (2018)	U	○	N/A	○	●	●	●	○						3	VL

Notes: ●, no; ○, yes; H, high; L, low; M, moderate; N/A, not applicable; U, unclear; VL, very low.

Table 7). Further, the main three outcomes reported by each intervention were identified.

4.2.1 | Towel materials

Seven studies compared the effects of traditional cotton towels and disposable towels (Gillis et al., 2016; Groven et al., 2017; Larson et al., 2004; Matsumoto et al., 2019; Nøddeskou et al., 2015; Schoonhoven et al., 2015; Veje et al., 2020).

Schoonhoven et al. (2015) reported that disposable towels slightly decreased the number of skin abnormalities compared with cotton towels, but no differences were found in significant skin lesions. As a result of the 12-week intervention, the SCH on patient's cheeks was higher when disposable towels were used instead of cotton ones. However, no differences were found in the other corporeal sites (Gillis et al., 2016). One study reported that disposable towels maintained SCH more effectively than cotton towels in the upper and lower limbs after a bed bath (Matsumoto et al., 2019). The high-quality systematic review by Groven et al. (2017) demonstrated an additional need for research.

There was no difference in the post-bed bath bacterial counts based on the use of both towels (Larson et al., 2004). There was also no significant difference in the reduction of the number of microorganisms in the groin and perineum (Veje et al., 2020).

Regarding the psychological effect on patients, disposable towels were highly satisfactory (Schoonhoven et al., 2015). There was no difference in bed bath satisfaction (Nøddeskou et al., 2015) and resistance based on the use of both towels (Groven et al., 2017;

TABLE 3 Characteristics and results of included studies that performed interventions regarding "towel materials" ($N = 7$)

Author (year)/ Country	Design	Participants	Interventions	Outcome measures	Main findings
Gillis et al. (2016)/ Belgium	RCT	163 residents in nursing homes (I = 117: mean age [*SE*] = 86 [1.5] years, C = 46: 82 [2.2] years)	I = Disposable bed bath (with use of "wash gloves") C = Traditional bed bath	● SCH (hand, leg and cheek)	As a result of the 12-week intervention, the SCH on patients' cheeks was higher for (I) as compared to (C) ($p = .02$). However, both methods had similar effects on the skin barrier function at the other corporeal sites.
Groven et al. (2017)/ Netherlands	Systematic review		I = Disposable bed bath C = Traditional bed bath	● Physiological outcomes related to hygiene and skin condition ■ Stakeholder-related outcomes ◊ Organizational outcomes	Only two high-quality studies showed that (I) was more effective than (C) regarding skin abnormalities and bath completeness. There were no differences between (I)–(C) in skin lesions, resistance for bed bath and cost. These results demonstrated an additional need for research because only a few high-quality studies that compared (I) to (C) were found.
Larson et al. (2004)/ USA	Crossover design	47 patients (IC = 47: mean age = 60.7 years) 40 nurses	I = Disposable bed bath C = Traditional bed bath	▲ Microbial counts (umbilicus and groin) ◊ Nurse satisfaction ◊ Costs ◊ Time and quality of a bed bath	There was no difference in post-bed bath total bacterial counts, regardless of whether (I) or (C) was used. Nurses preferred (I) to (C) in items of overall preference (e.g. ease of use, less time, patient's comfort and fewer supplies, $p < .001$). The total time and costs did not differ between (I)–(C).
Matsumoto et al. (2019)/Japan	Crossover design	62 healthy elderly people (IC = 62: mean age [*SD*] = 73.1 [4.8] years)	I = Disposable bed bath C = Traditional bed bath	▲ Resident skin bacteria ▲ *Staphylococcus aureus* ● SCH ● TEWL ■ Relaxation levels (Profile of Mood States Second Edition: POMS2 short form and evaluation of towel materials)	Both (I) and (C) significantly decreased resident skin bacteria ($p < .05$). (I) significantly decreased the number of *Staphylococcus aureus* and maintained SCH more effectively than (C) in the upper and lower limbs after a bed bath ($p < .05$). (I) was also more effective than (C) in facilitating participants' relaxation.
Nøddeskou et al. (2015)/ Denmark	Crossover design	58 residents (IC = 58: mean age = 73 years)	I = Disposable bed bath C = Traditional bed bath	◊ Duration and quality ◊ Cost ◊ Nurse satisfaction (Likert scale from 1–10.) ■ Patient satisfaction (Likert scale from 1–10.)	The total quality of bed bath was very high, with no differences between (I)–(C). There were no differences in the cost and patient satisfaction. (I) required significantly less time ($p < .001$) and was preferred by nurses ($p < .01$) to (C).

(Continues)

TABLE 3 (Continued)

Author (year)/ Country	Design	Participants	Interventions	Outcome measures	Main findings
Schoonhoven et al. (2015)/ Netherlands	RCT	500 residents in nursing homes (I = 290: mean age [SE] = 81.8 [8.7] years, C = 210: 83.3 [7.5] years) 275 nurses	I = Disposable bed bath C = Traditional bed bath	● Any skin abnormalities ● Significant skin lesions ■ Resident satisfaction (Likert scale from 0–10.) ◊ Nurse satisfaction (Likert scale from 0–10.) ◊ Cost ◊Resistance: agitation, aggression and discomfort	Any skin abnormalities (including clinically non-related signs such as discolorations) in (I) slightly reduced over time, while those in (C) slightly increased ($p = .04$). The time courses in the prevalence of significant skin lesions were equal between (I)–(C). Sixty-one per cent of nurses preferred to replace (I) with (C). Residents who received (I) were reported experiencing skin cleanliness (94% of them felt this was sufficient or good) and refreshment (83% of them felt this was sufficient or good). There were no differences between (I)–(C) regarding patients' resistance and costs.
Veje et al. (2020)/ Denmark	Crossover design	58 patients (IC = 58: Median age [range] = 77 [38–96] years)	I = Disposable bed bath C = Traditional bed bath	▲ Microorganism (groin and perineum) that potentially could cause hospital-acquired urinary tract infections	The results showed a significant reduction in the amount of microorganisms after (C) ($p = .0001$) and (I) ($p = .0148$). There was no difference in the decrease of microorganisms between (I)–(C)

Notes: ■, outcome for comfort enhancement; ▲, outcome for skin cleanliness; ◊, outcome for the others; ●, outcome for skin integrity; C, control group; I, intervention group; SCH, stratum corneum hydration; TEWL, transepidermal water loss.

Schoonhoven et al., 2015). Nurses preferred the disposable towels (Larson et al., 2004; Nøddeskou et al., 2015; Schoonhoven et al., 2015).

4.2.2 | Thermal stimulation

Three studies performed interventions regarding differences in thermal stimulation (Shishido et al., 2017; Shishido & Yano, 2017; Silva et al., 2016).

The TEWL in elderly participants' forearm increased significantly when the bed bath did not involve applying a hot towel for 10 s (AHT10s). However, there was no such significant TEWL increase when the bed bath involved AHT10s (Shishido & Yano, 2017).

Of the three AHT durations, AHT10s on the back showed the highest subjective comfort (Shishido et al., 2017). The bed bath that involved AHT10s raised the skin surface temperature of healthy adults' backs and the elderly adults' forearms, providing them warmth and comfort (Shishido et al., 2017; Shishido & Yano, 2017).

Silva et al. (2016) compared bed baths for infarcted patients with a constant water temperature of 40°C and a constant temperature of 42.5°C. Both temperatures were safe, but a bed bath with a constant water temperature at 42.5°C significantly increased SpO_2 and axillary temperature and reduced heart rate by 1%.

4.2.3 | Wiping

Four studies performed interventions regarding differences in wiping (Aoki et al., 2019; Konya et al., 2020; Konya, Yamaguchi, et al., 2020; Matsumoto et al., 2018).

Neither ordinary nor weak pressure applied by clinical nurses negatively affected the skin barrier function, and they did not have significantly different effects (Konya, Yamaguchi, et al., 2020).

Both oily and aqueous dirt can be removed sufficiently by wiping three times with a pressure level of 10 mmHg or more; wiping three times with 10.0–27.4 mmHg is sufficient for dirt removal without impairing the skin barrier function of healthy adults (Konya et al., 2020). A wiping method for dirt removal that used circular motions by shifting outward from the centre was more effective than methods that wiped from the periphery to the centre, or vice versa (Matsumoto et al., 2018). However, there were no significant differences for cleaning agent removal among these wiping directions (Aoki et al., 2019).

Wiping pressure had a significant association with the sense of having dirt removed in healthy adults' subjective evaluations (Konya, Yamaguchi, et al., 2020).

4.2.4 | Chemical products

Four studies performed interventions regarding the presence or absence of, and differences in, chemical products (Cowdell et al., 2020; Hayama et al., 2015; Nerandzic et al., 2013; Ogai et al., 2017).

TABLE 4 Characteristics and results of included studies that performed interventions regarding "thermal stimulation" ($N = 3$)

Author (year)/ Country	Design	Participants	Interventions	Outcome measures	Main findings
Shishido et al. (2017)/Japan	Crossover design	Experiment A: 20 healthy adults (mean age [*SD*] = 21.6 [0.7] years) Experiment B: 21 healthy adults (IC = 21: mean age [*SD*] = 21.7 [0.8] years	Experiment A: Determination of the AHT durations (10, 15 and 20 s) Experiment B: I = AHT for E seconds + Wiping 4 round trip to the back + Drying C = Wiping 4 round trip to the back + Drying	◊ Skin surface temperature ◊ Towel surface temperature ■ Subjective evaluations (Likert scale from 1–4)	Of the three AHT durations (10, 15 and 20 s), AHT10s on the back showed the highest subjective comfort. For (I), AHT10s raised the skin surface temperature of healthy adults' backs and provided comfort ($p = .047$) and warmth ($p = .001$). However, for (C), it significantly reduced the skin surface temperature ($p < .001$).
Shishido and Yano (2017)/Japan	Crossover design	21 residents in long-term care health facilities (IC = 21: mean age [*SD*] = 84.8 [7.4] years)	I = Applying a hot towel for 10 s + Wiping 3 times to the forearm + Drying C = Wiping 3 times to the forearm + Drying	● SCH ● TEWL ■ Subjective evaluations (Likert scale from 1–4) ◊ Skin surface temperature	The TEWL in elderly participant's forearms increased significantly when bed bath involved (C) ($p = .035$), but there was no such increase when bed bath involved (I). The latter provided all the residents with subjective warmth, comfort, and raised skin surface temperature.
Silva et al. (2016)/ Brazil	Crossover design	20 patients who had acute myocardial infarction (AMI) (IC = 20: mean age [*SD*] = 62.0 [9.0] years)	I1 = Bed bath with constant water temperature at 40.0°C I2 = Bed bath with constant water temperature at 42.5°C	◊ Pulse oximetry ◊ Heart rate ◊ Axillary temperature	The SpO_2 and axillary temperature were higher after (I2) ($p < .05$) when compared with (I1). (I2) reduced heart rate by 1% ($p = .01$), and was more favoured than (I1) regarding SpO_2, heart rate and axillary temperature in infarcted patients.

Notes: ■, outcome for comfort enhancement; ▲, outcome for skin cleanliness; ◊, outcome for the others; ●, outcome for skin integrity; AHT, applying a hot towel; C, control group; I, intervention group; SCH, stratum corneum hydration; TEWL, transepidermal water loss.

TABLE 5 Characteristics and results of included studies that performed interventions regarding "wiping" ($N = 4$)

Author (year)/ Country	Design	Participants	Interventions	Outcome measures	Main findings
Aoki et al. (2019)/ Japan	Pretest–post-test design with compared groups	18 healthy adults (I1C = 6, I2C = 6, I3C = 6: aged 21–22 years)	C = "Protective cleaning method" + washing for 20 s I1 = "Protective cleaning method" + wiping in a direction from the periphery to the centre I2 = "Protective cleaning method" + wiping in a direction from the centre to the periphery I3 = "Protective cleaning method" + wiping in circular motions shifting outward from the centre	▲ Cleaning agent residual index at the hair root and bulb in lateral surface of leg	There were no significant differences for cleaning agent removal (taken from the hair follicle: roots and bulbs) among wash-away methods or the wiping-off methods that differ in wiping directions.
Konya et al. (2020)/ Japan	Crossover design	50 healthy adults (I1I2 = 50: mean age [*SD*] = 22.6 [1.9] years)	I1 = Adhesion of oily pseudo-dirt + wiping 3 times with wiping pressure classified into 6 randomly assigned categories I2 = Adhesion of aqueous pseudo-dirt + wiping 3 times with wiping pressure classified into 6 randomly assigned categories	▲ Dirt removal rate by a digital image colour analysis ● TEWL ● SCH	Both oily and aqueous dirt were removed sufficiently by wiping three times, with a pressure level of 10 mmHg or more; wiping three times with 10.0–27.4 mmHg would be sufficient for dirt removal without impairing the healthy adults' skin barrier function.
Konya, Yamaguchi, et al. (2020)/Japan	Crossover design	Phase I: 55 nurses Phase II: 28 healthy adults (I1I2 = 28: mean age [*SD*] = 21.8 [1.4] years	I1 = Wiping 3 times with ordinary pressure (23–25 mmHg) to the forearm I2 = Wiping 3 times with weak pressure (12–14 mmHg) to the forearm	Phase I: Wiping pressure provided by nurses Phase II: ● TEWL ● SCH ▲ Adenosine triphosphate ■ Subjective evaluations (Likert scale from 1–4)	Neither (I1:23.8 [1.3] mmHg: mean [*SE*]) nor (I2: 13.1 [0.9] mmHg) applied by clinical nurses negatively affected the skin barrier function or have significantly different effects on skin integrity and cleanliness. Wiping pressure had a significant association with the sense of having dirt removed in participants' subjective evaluations ($p = .036$); some participants felt that even the application of weak pressure was slightly painful.
Matsumoto et al. (2018)/Japan	Crossover design	5 healthy adults in their 20 s (I1I2I3C = 5)	C = "Protective cleaning method" + washing for 20 s I1 = "Protective cleaning method" + wiping in a direction from the periphery to the centre I2 = "Protective cleaning method" + wiping in a direction from the centre to the periphery I3 = "Protective cleaning method" + wiping in circular motions shifting outward from the centre	▲ Dirt in sulcus cutis ▲ Dirt in skin surface	Compared with the wash-away method, the wiping-off method was more effective in skin dirt removal from skin surfaces. Furthermore, wiping methods using circular motions by shifting outwards from the centre spread less skin dirt and were most effective for skin dirt removal.

Notes: ■, outcome for comfort enhancement; ▲, outcome for skin cleanliness; ◊, outcome for the others; ●, outcome for skin integrity; C, control group; I, intervention group; SCH, stratum corneum hydration; TEWL, transepidermal water loss.

TABLE 6 Characteristics and results of included studies that performed interventions regarding "chemical products" ($N = 4$)

Author (year)/Country	Design	Participants	Interventions	Outcome measures	Main findings
Cowdell et al. (2020)/ UK	Systematic review	People aged 60 years or older in hospital and residential care settings	I = Different washing practices and emollients (moisturizers) for maintaining skin integrity. C = Usual care or no treatment	● Frequency of skin damage ● Frequency of cutaneous reaction ● TEWL ● SCH ● Erythema ● Skin dryness ● Itch ● Corneosurfametry ● Skin pH ● Types and concentrations of SC lipids ▲ Resident microbes	(I) for elderly residents had more effective outcomes related to skin dryness than (C). However, the evidence level of (I) was very low, which cannot help determine the most effective practice regarding prevalence of skin damage or side effects.
Hayama et al. (2015)/ Japan	Crossover design	7 patients who have senile xerosis (IC = 7: mean age [*SD*] = 88.0 [6.0] years)	I = Bed bath + treatment with a heparinoid-containing agent C = Bed bath	● SCH	Treatment using heparinoid-containing moisturizer after bed bath significantly and continuously maintained SCH, while a bed bath alone slightly increased senile xerosis ($p < .05$). These findings indicate that (I) is effective for patients with senile xerosis.
Nerandzic et al. (2013)/USA	Pretest–post-test design with compared groups	47 patients with *Clostridium difficile* infection (CDI) (I = 21, C = 26)	I = Bed bath with a sporicidal electrochemically generated hypochlorous acid solution (Vashe®) C = Bed bath with soap	▲ Removal of *Clostridium difficile* spores from the skin	(C) Did not decrease the positive skin cultures for the patients ($p = .5$), while (I) significantly decreased skin contamination ($p = .0001$).
Ogai et al. (2017)/ Japan	Pretest–post-test design with compared groups	14 healthy adults (A = 5, B = 5, C = 4: aged 20–21 years) * The participants were classified into 3 groups corresponding to the cleaning agents (A, B and C) that can be removed by both washing and wiping.	I1: WASH = using the cleaning agents* + "protective cleaning method" + washing for 20 s I2: WIPE = using the cleaning agents* + "protective cleaning method" + wiping 5 round trips	● TEWL ● SCH ● Skin pH ● Semi-quantification of skin ceramide content	There were no differences in the effects on skin barrier function or ceramide content between (I1)–(I2) for cleaning agents that can be removed using both methods.

Notes: ■, outcome for comfort enhancement; ▲, outcome for skin cleanliness; ◊, outcome for the others; ●, outcome for skin integrity; C, control group; I, intervention group; SCH, stratum corneum hydration; TEWL, transepidermal water loss.

Hygiene and emollient-related interventions to maintain the skin integrity of elderly residents had more effective outcomes with regard to skin dryness, as compared with standard care or no interventions (Cowdell et al., 2020). The treatment using heparinoid-containing moisturizer after bed bath significantly and continuously maintained SCH, while a bed bath alone slightly increased senile xerosis (Hayama et al., 2015). There were no differences in the effects for skin barrier function or ceramide content between the washing and wiping procedure of cleaning agents that can be removed from both methods (Ogai et al., 2017).

4.3 | Methodological quality

Only four of the included studies were of high quality, with most being of moderate quality (Table 2). Overall, there were few RCTs, and information regarding participant randomization, concealment and blinding was limited, suggesting a high risk for selection and performance bias. The main reasons for insufficient statistical or power analyses were the lack of a sample size calculation. Only eight measured the outcomes reliably while the others demonstrated high detection, instrument and measurement bias. Examining publication bias was impossible because many variations in the outcome measures and participants existed, and the sample sizes were small.

5 | DISCUSSION

Although bed baths are fundamental to nursing care and frequently performed in clinical practice, safe and effective methods that support skin integrity, cleanliness and enhanced comfort have not been clarified. This is the first systematic review to our knowledge to address this issue comprehensively.

5.1 | Bed bath methods for skin integrity

The importance of skin integrity is generally accepted for the fields of skin care because it is a quality indicator of patient care (Lichterfeld et al., 2015), and maintaining skin integrity with daily routine skin care, such as a bed bath, indicates higher cost-effectiveness than wound treatment (Flanagan et al., 2014).

The high-quality study showed that although the number of skin abnormalities decreased using a disposable towel, compared to using a traditional cotton towel, there were no differences in the number of significant skin lesions over time between the use of the two towels (Schoonhoven et al., 2015). However, some studies of moderate quality showed that disposable towels also effectively maintained the SCH compared to cotton towels (Gillis et al., 2016; Matsumoto et al., 2019) because they contain moisturizing ingredients. Therefore, we could not clearly determine the superiority or inferiority of any towel material. As a method of selecting towel materials to maintain skin integrity, we can synthesize and suggest that bed baths using a disposable towel are not inferior to those using a cotton towel because no study has shown that cotton towels are superior regarding skin integrity. These findings proven as the effects of the multiple intervention for elderly inpatients and residents in nursing homes.

There was evidence that bed baths with AHT10s would protect the skin barrier function from friction irritation more than those without (Shishido & Yano, 2017), as AHT10s can increase the skin's suppleness. This result has implications for patients with particularly severe dryness. At present, the effects of this practice have been observed among healthy elderly persons in nursing homes; its effect on inpatients is not clear. It has been reported that elderly inpatients have severe skin dryness (Paul et al., 2011); thus, expanding the applicable population for this practice should be prioritized in the future.

Extremely strong wiping friction in bed baths may cause skin tears (Bryant & Rolstad, 2001). Even though wiping pressure and number of wipes directly cause friction irritation, recommendation suggested by previous studies is very vague. Konya et al. (2020) suggested that wiping three times with 10.0–27.4 mmHg is sufficient for dirt removal without impairing the skin barrier function of healthy adults. It is expected that the optimal wiping pressure will be elucidated from this range, but research is currently limited to fundamental studies for healthy adults. A clinical study, including sufficient statistical power for elderly inpatients with vulnerable skin, would be useful for determining best practices for wiping pressure.

Soaps and some cleansers tend to alkalize the skin surface, which would negate the protective effects of the acid mantle and the balance of resident flora or natural moisturizing factors (Voegeli, 2008). This is a suggested cause of disturbed skin barrier function. Therefore, the use of cleansers and moisturizers that account for skin integrity has been investigated. Only one study examined the use of moisturizers in relation to bed baths (Hayama et al., 2015). Heparinoid-containing moisturizers, which this study showed to be effective, are already used in hospitals for patients with dry skin. When the study field is extended to incorporate skin care, it is recommended that mild cleansers with a pH close to 4.5–5.7 (Lichterfeld et al., 2015) and humectants (Cowdell et al., 2020) are used. Leave-on products comprising lipophilic-humectant are effective for improving skin barriers and dry skin among the older people (Lichterfeld-Kottner et al., 2020). In addition, nurses must carefully assess the medical history of patients undergoing bed bath in order to choose the correct detergents and emollients. Specifically, therapy guidelines for atopic dermatitis recommend a regular emollient application and use of emollient bath oils and non-comedogenic soap substitutes to prevent triggering symptoms as basic therapy for a disturbed skin barrier function (Damiani et al., 2019). Unfortunately, few studies exist regarding high-quality chemical products for bed baths. However, evidence regarding best practices has been clinically examined in the field of skin care. Such practices can be applied to the bed bath for elderly people in hospital and residential care settings with dry skin.

TABLE 7 Characteristics and results of included studies that performed interventions regarding "others" ($N = 7$)

Author (year)/ Country	Design	Participants	Interventions	Outcome measures	Main findings
Coyer et al. (2011)/ Australia	Analytical cross-sectional study (Phase 1)	539 nurses in 4 intensive care unit (ICU) of hospital		◊ Questionnaire (timing, frequency, duration and cleansing agents used)	Thirty per cent of the bed baths were performed between 02.00–06.00 hr, while 36.2% took 15–30 min. Cleansing agents of pH balanced soap or liquid soap and water (71%) were used more than chlorhexidine impregnated towels (16.1%) or other agents such as disposable towels (12.2%). Most of the bed baths (64.4%) did not apply emollients after this care.
Jacq et al. (2018)/ France	Pretest–post-test design with compared groups	60 mechanically ventilated patients in intensive care unit of hospital (median age[range] = 69.0 [60–80] years)	I = Bed bath with music intervention C = Bed bath with no music	◊ The Behavioral Pain Scale (BPS): Pain defined as a BPS score ≥5	In both groups, before bed bath, the patients experienced no pain. After bed bath, 88% of patients felt pain. The total bathing time reached the maximum BPS and BPS ≥ 5, and (I) was significantly less effective than (C) ($p = .005$, $p < .001$, respectively).
Jury et al. (2011)/ USA	Cohort Study	74 patients with clostridium difficile infection (CDI) (I1 = 10, I2 = 64: mean age[range] = 66.0 [31–89] years)	I1 = Shower I2 = Bed bath	▲ Removal of *Clostridium difficile* spores from the skin	A significant reduction in the proportion of positive culture in the whole body (arm, hand, chest, abdomen and groin) and number of spores acquired on the whole body were found after (I1) ($p = .03$; $p = .04$, respectively), but not after (I2).
Lopes et al. (2010)/ Brazil	Crossover design	71 patients with acute myocardial infarction in the coronary units of the Heart Institute (I1I2 = 71: mean age[range] = 58.8 [53–61] years)	I1 = Shower (took their bath without direct assistance, though they were under supervision) I2 = Bed bath (assisted by a nursing professional)	■ State-Trait Anxiety Inventory (STAI) ◊ Vital signs	Patients with acute myocardial infarction felt more anxious during (I2) as compared to during (I1) before and 20 min after bathing ($p < .0001$). However, high blood pressure may affect these results because hypertensive patients were more anxious about bathing than non-hypertensive patients.
Lopes et al. (2013)/ Brazil	Crossover design	71 patients with acute myocardial infarction in the coronary units of the Heart Institute (I1I2 = 71: Mean age = 58.8 years)	I1 = Shower (took their bath without direct assistance, though they were under supervision) I2 = Bed bath (assisted by a nursing professional)	■ Semantic Differential Scale (e.g. patients' affective attitudes, opinions, perceptions, social image, personality and preferences)	Patients included in (I1) had significantly more positive perceptions than in (I2). However, patients who underwent prior hospitalization showed fewer positive perceptions towards both types of bathing than those who underwent hospitalization for the first time.
Matsumura and Fukai (2018)/ Japan	Analytical cross-sectional study	669 nurses working on a ward in 11 hospitals		◊ Questionnaire (type and number of the tools used to complete bed bath, type of complete bed bath mainly provided, actual frequency, nurse's satisfaction and patient's satisfaction)	The following results were identified: (1) bed baths with steamed towels were the most common method (77.7%); (2) half or more of the nurses were not satisfied with their own practices and they recognized that inpatients were also not satisfied; and (3) the nurses were not satisfied with their own practices because of their busy task schedules, staff shortages and insufficient effects of the bed baths.

(Continues)

TABLE 7 (Continued)

Author (year)/ Country	Design	Participants	Interventions	Outcome measures	Main findings
Sloane et al. (2004)/ USA	RCT	69 residents with agitation in nursing homes (I1I2 = 46: Mean age [SD] = 86.0 [8.6] years, C = 23:86.9 [6.1] years)	I1 = Person-centred showering I2 = Person-centred bed bath with no-rinse soap C = Showering without person-centred training	◊ Resistance: agitation, aggression, and discomfort (Care Recipient Behavior Assessment: CAREBA) ▲ Skin microbiology ● Any skin abnormalities (debris) ◊ Bath completeness and duration	All measures related to agitation and aggression decreased significantly in both (I1) and (I2), but not in (C) ($p < .001$). Discomfort scores also decreased significantly in (I1) and (I2) ($p < .001$), but not in (C). Although (I1) and (I2) indicated similar agitation/aggression reduction, (I2) showed lesser discomfort ($p = .003$). Bath duration increased significantly (average: 3.3 min) in (I1) but not in (I2). Both (I1) and (I2) improved skin conditions, such as debris, and decreased colonization of potentially pathogenic bacteria.

Notes: ■, outcome for comfort enhancement; ▲, outcome for skin cleanliness; ◊, outcome for the others; ●, outcome for skin integrity; C, control group; I, intervention group; SCH, stratum corneum hydration; TEWL, transepidermal water loss.

5.2 | Bed bath methods for skin cleanliness

Skin cleanliness is one of 14 components of Virginia Henderson's Need Theory (Henderson, 1966), and removing skin dirt with skin care, including a bed bath, is an integral part of nursing practice (Lichterfeld et al., 2015).

Regarding towel material, the use and management of cotton towels to avoid cross-contamination or outbreak have been considered (Skewes, 1996), and differences in the cleaning effect of towel materials have been examined. However, the results of most of the studies for adult and elderly patients show that the cleaning and bacterial removal effects of cotton and disposable towels are similar. Therefore, it is thought that skin cleanliness can be maintained by either method, if management methods such as towel selection and disinfection are employed.

Friction irritation, such as wiping pressure and the number of wipes, is directly related to the degree of skin dirt removal. Konya et al. (2020) reported that wiping three times with ≥10 mmHg could sufficiently remove oily dirt, and wiping once even with ≥5 mmHg could almost completely remove aqueous dirt. Therefore, even without exerting a strong pressure, wiping at least three times would sufficiently improve skin cleanliness for adults. Regarding wiping direction, the wiping method using circular motions by shifting outwards from the centre was the most effective method for skin dirt removal (Matsumoto et al., 2018), but the sample size was very small. Attrition and measurement bias were also particularly high in this study. Therefore, it may be difficult to offer evidence that can be applied in clinical practice.

5.3 | Bed bath methods for enhancing comfort

Patient comfort is regarded as "an individualized, holistic experience and a source of patient satisfaction and well-being (Lorente et al., 2018)," and this concept has been historically important in nursing. Notably, bed baths are the most effective measures available to nurses in terms of their role in providing comfort to patients (Shibutani, 2018). Therefore, it is important for clinical nurses and researchers to determine how to enhance patients' comfort.

In the present age, efficiency of care has been required as advanced medical care has progressed, and many nurses are busy as a result of tight schedules and lack of staff (Matsumura & Fukai, 2018). As a result, they have not been able to provide high-quality bed baths to provide comfort and satisfaction to both patients and nurses (Matsumura & Fukai, 2018). Because AHT10s has a significantly short duration and provides warmth and comfort to healthy and elderly adults' forearm and back (Shishido & Yano, 2017), it may solve the dilemma of bed baths in clinical practice. Furthermore, by adjusting the hot water temperature to 40–42.5°C depending on the patient's preference and condition (Silva et al., 2016) and combining with dry wiping to avoid maceration and undue cooling, it seems possible to efficiently provide warmth and comfort to the patient.

There is no unified view of the psychological effects of the towel materials. A moderate quality study recommended a disposable towel in consideration of nurse satisfaction, time and cost in addition to patient satisfaction (Larson et al., 2004). However, a high-quality systematic review concluded that there is no difference between materials because previous studies examining the difference in towel materials did not compare the nurses' and patients' satisfaction based on disposable and cotton towels (Groven et al., 2017). There is no gold standard that can evaluate patients' subjectivity regarding their opinions about bed baths. However, a recent qualitative study aimed to understand and explore patients' experiences of bed baths with water and soap or disposable wipes (Veje et al., 2019). In this study, patients preferred bed baths with water and soap, but the use of disposable wipes was preferable and convenient in certain circumstances, such as when a patient had diarrhoea or pain. Originally, such a qualitative study should first be used to develop a valid and reliable scale reflecting patients' subjectivity or preference of bed bath. At present, there is no instrument that can evaluate multi-faceted patients' subjectivity and preferences such as the sensation of being wiped, warmth and comfort. Additional work is required to understand the habits, patient subjectivity and preferences of towel material.

5.4 | Recommendations for research

We recommend three points for future research on bed baths. First, it should describe more detailed bed bath methods. This will not only ensure the reproducibility of the intervention of bed baths and facilitate intervention control, but it will also be easier to compare intervention effects. In clinical practice, it will be easier to apply effective bed bath methods for clinical nurses.

Second, we recommend regarding outcome measures. As for skin integrity, most of the studies used the gold standards for skin barrier function measurements such as TEWL and SCH (Martini et al., 2018). In addition to this, we believe that measures will be easier to apply in clinical settings if more common clinical scores are used increasingly, such as skin dryness and lesions, as outcome measures. Regarding skin cleanliness, most of the studies evaluated the increase and decrease in the number of microorganisms. Furthermore, to precisely evaluate the "degree of dirt removal" based on different bed bath methods, the method of purposely adding dirt to the skin and evaluating the removal rate is considered more effective, as found in three studies (Aoki et al., 2019; Konya et al., 2020; Matsumoto et al., 2018). Regarding the subjective evaluation (e.g. patients' comfort) of the bed bath, there was less evidence compared with that of skin integrity and cleanliness. This seems to be because the questionnaires used in the studies were created by the researchers for their individual studies, and the outcome measures are not unified. A psychometric review of instruments to assess hospitalized patients' comfort (Lorente et al., 2018) suggested that there is no instrument that can be recommended for questionnaires measuring patients' comfort. Therefore, this review suggests that such instruments need to be developed for the establishment of evidence regarding bed baths.

Finally, we propose a methodological study. A rigorous and accurate study design (i.e. a RCT) is necessary to minimize the risk of bias due to methodological quality. Given our findings, future studies should conduct and report appropriate procedures regarding randomization, concealment and blinding of bed bath methods (e.g. the use of central randomization). Outcomes should be measured reliably, with the number of assessors, assessment training and intra-rater or inter-rater reliability being recognized as important elements. The importance of sample size calculation should be recognized, and appropriate statistical analysis should be performed. In addition, it is necessary to verify the moderate-quality results obtained from fundamental studies of healthy adults in a large-scale (including a large sample size, multiple interventions and long study duration) clinical study targeting elderly patients and patients with specific diseases.

5.5 | Limitations

This study has several limitations. First, we did not appraise the risk of reporting bias and could not contact the authors of the included studies about criterion ratings of "unclear" in the JBI checklist. Therefore, it was not possible to consider whether the authors reported all study results or intervention methods related to critical appraisal.

Second, the search strategy in this review could not search by setting the keywords of the patients and synthesizing the bed bath methods according to the patient characteristics. This is due to the fact that there are many quasi-experimental studies about bed baths among healthy adults, and there is little knowledge of bed baths' effects on patients. Although some may consider our setting keywords to affect the adaptability of the search results, by including all the subjects, we could comprehensively and systematically evaluate the bed bath methods.

6 | CONCLUSION

This systematic review evaluated and synthesized the effectiveness of evidence-based bed bath methods for skin integrity, skin cleanliness and comfort enhancement in consideration of the methodological evidence level of studies. As a result of narrative synthesis, we found the following: (1) disposable towels were as effective as cotton towels in terms of removing bacteria and not causing significant skin lesions, (2) applying a hot cotton towel to the skin before wiping maintained the skin barrier function and provided warmth, (3) skin could be cleaned effectively even when applying weak pressure while wiping and (4) treatment with moisturizer after the bed bath contributed to skin integrity. The findings in points (1) and (4) were proven as the effects of the multiple intervention for elderly inpatients and residents. The findings in point (2) were addressed as the effect of a single intervention for healthy adults and elderly residents in a nursing home. Moreover, the findings in point (3) were tested as

the effect of a single intervention only in healthy adults. Although towels, moisturizers and bed bath methods have been examined, the available evidence is inadequate for establishing best practices because only four of the included 25 studies were of high quality. It is necessary to verify empirical research with rigorous methodology involving elderly inpatients and to develop instruments that measure patients' comfort.

7 | RELEVANCE TO CLINICAL PRACTICE

The bed bath method suggested in this review can be safe and effective for adults in terms of skin integrity, skin cleanliness and comfort enhancement. Nurses and caregivers may apply these results to daily care, especially for elderly people with high skin vulnerability who are frequently given bed baths. This would help standardize and improve the quality of nursing care.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

IK and RY designed the study and wrote the manuscript. IK, KN and RY collected the data and analysed the data.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the supplementary material of this article.

ORCID

Issei Konya https://orcid.org/0000-0002-7274-5955
Rika Yano https://orcid.org/0000-0002-5243-8763

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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